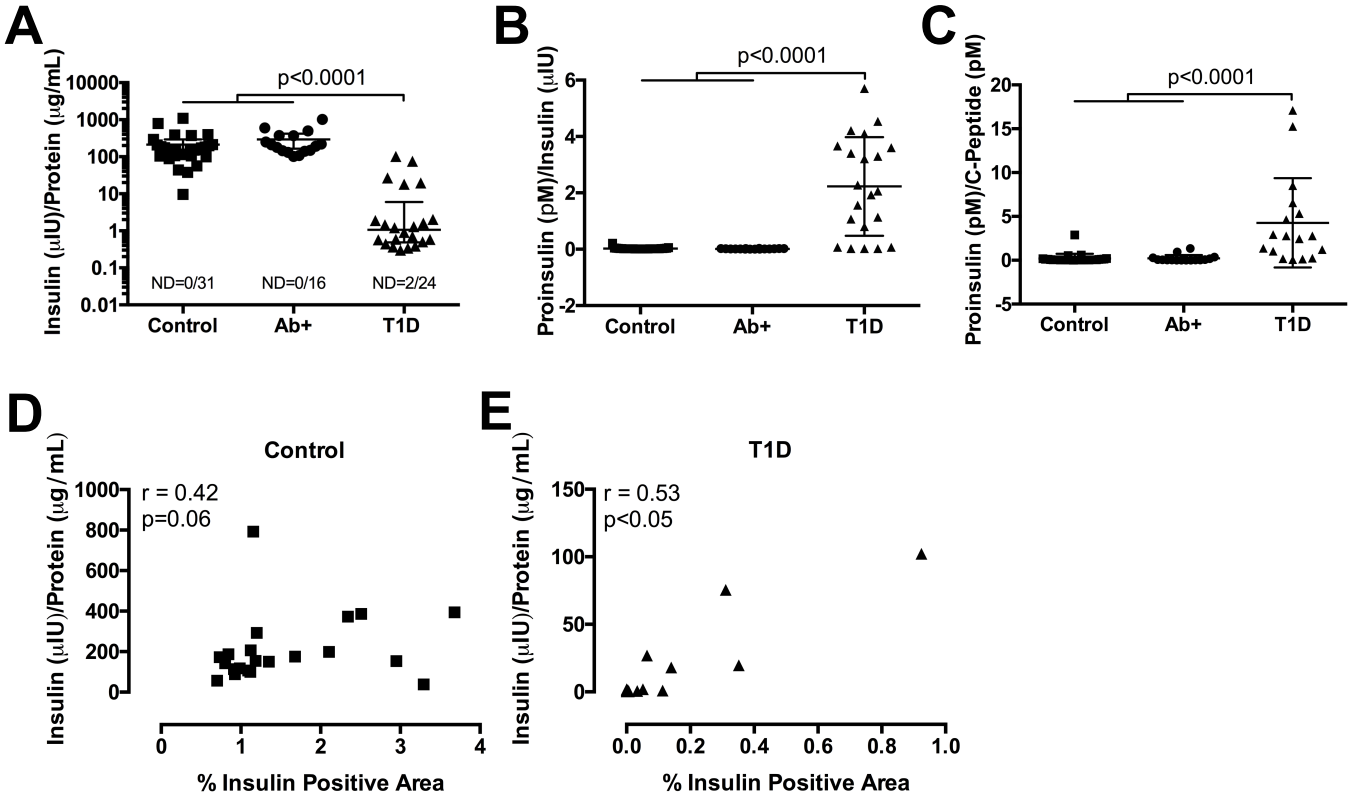
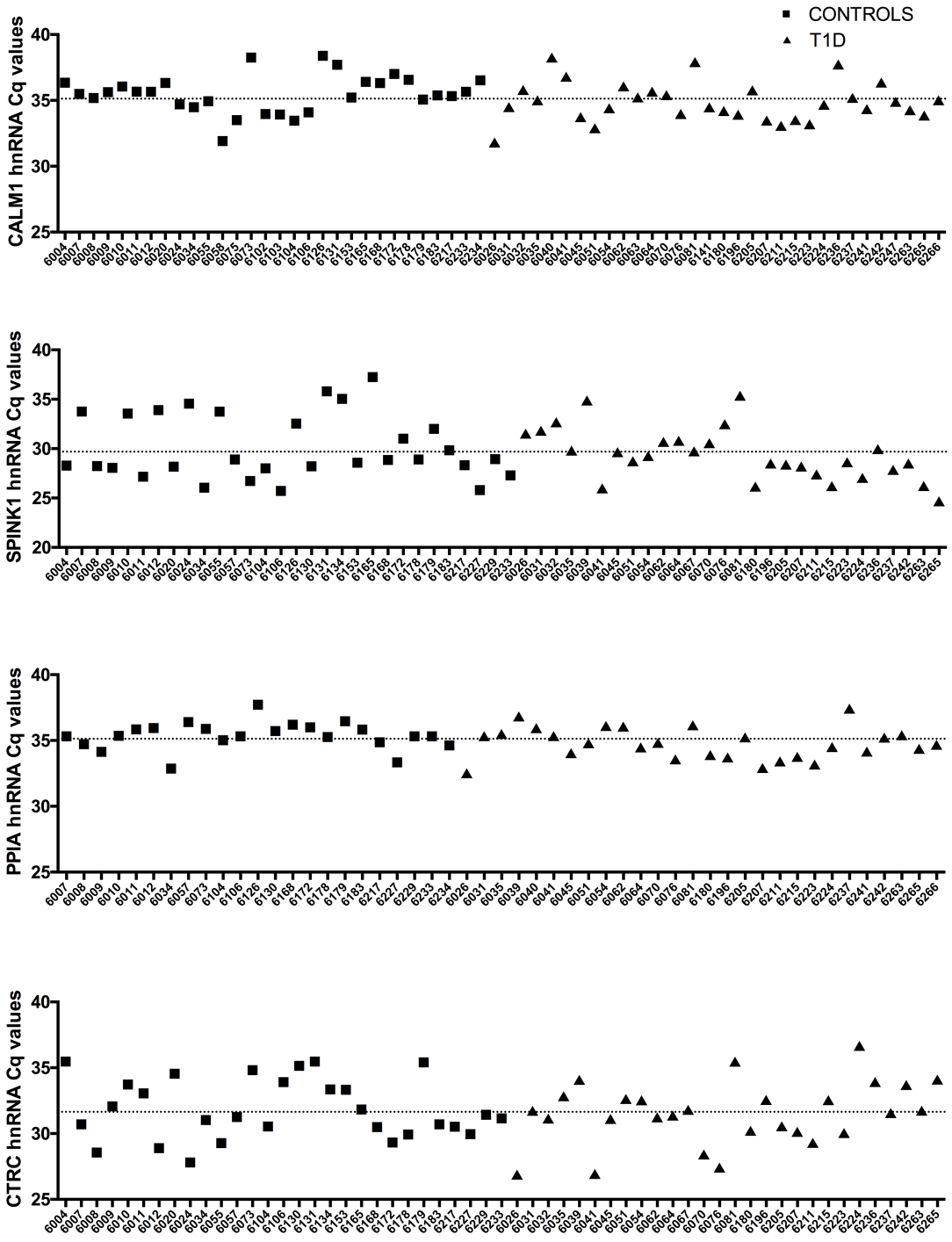
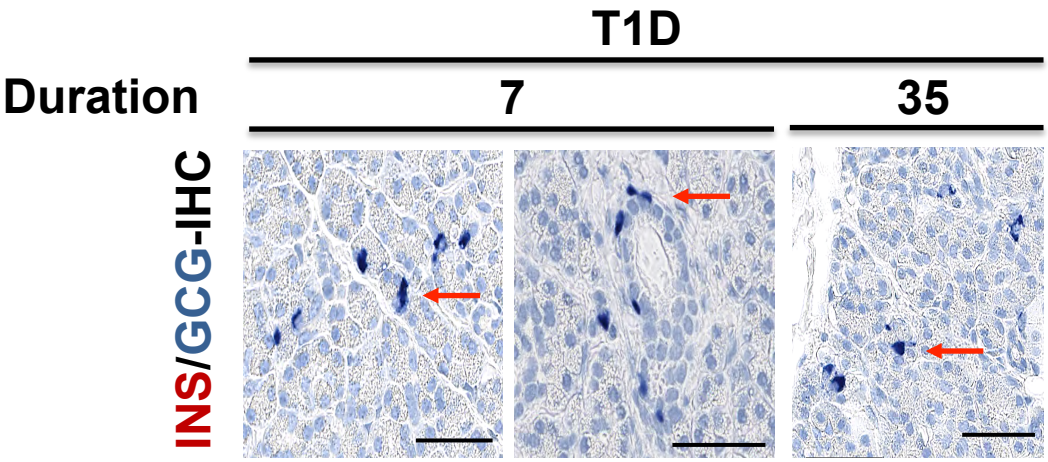
Supplemental Figure 1



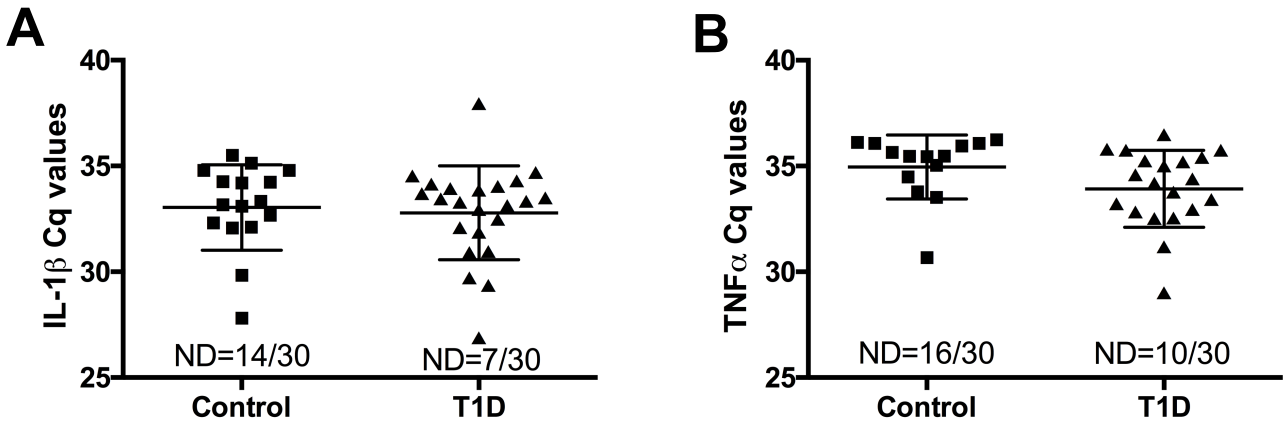
Supplemental Figure 2



Supplemental Figure 3



Supplemental Figure 4



Supplemental Figure Legends

Supplemental Figure 1. Extracted proinsulin, insulin, and C-Peptide ratios, Related to Figure 2.

(A-C) Proinsulin, insulin, and C-peptide measured by ELISA from pancreas protein extracts from control, autoantibody positive (Ab+), and type 1 diabetes (T1D) organ donors. (A) Extracted insulin is shown with a logarithmic y-axis as compared to the linear scale shown in Figure 2A (ND = not detected / examined is noted on the graph). (B) Proinsulin/Insulin (μInternational Units (μIU)) and (C) Proinsulin/C-Peptide ratios were compared via Kruskal-Wallis with Dunn's post-test (p-values indicated on the figure).

(D-E) Pancreas sections were stained for insulin via IHC and scanned into an online digital pathology system (Aperio). Fractional insulin area was determined using Indica Labs, Inc image analysis software (Corrales, NM). Percent insulin positive area was plotted versus the extracted insulin/total protein levels (μInternational Units (μIU)) for (D) control (N=21) and (E) T1D donors (N=21) and statistically analyzed using the Spearmans correlation with p-values indicated on the figure.

Supplemental Figure 2. Anaylysis of promoter activity from human pancreas, Related to Figure 2.

RNA (free of genomic DNA) was isolated from frozen human pancreatic tissue and evaluated by real time qPCR using an exon derived primer and a primer in the adjacent intron to evaluate hnRNA levels, thus evaluating promoter activity. hnRNA Cq values for

control and T1D pancreata for CALM1, SPINK1, PPIA and CTRC hnRNA were evaluated.

Supplemental Figure 3. Insulin and glucagon immunohistochemistry in type 1 diabetes (T1D), Related to Figure 3. Pancreas sections from two organ donors with T1D were stained for insulin (INS, red) and glucagon (GCG, blue). Left two panels are nPOD 6070; right panel is nPOD 6031. Donor T1D durations (years) are indicated in the figure. Scale bars represent 50 μm. Red arrows indicate single glucagon positive cells located in the exocrine tissues and the absence of insulin in this field of view.

Supplemental Figure 4. Evaluation of cytokine gene expression in human pancreas, Related to Figure 2.

RNA was extracted from frozen human pancreatic tissue and evaluated by real time qPCR. Cq values for control and T1D pancreata for (A) IL-1β and (B) TNFα. Statistical analyses were not performed due to the number of Control and T1D samples with undetectable RNA.

Supplemental Tables

Table S1. Related to Excel File Table S1, Related to STAR Methods. Network for Pancreatic Organ donors with Diabetes (nPOD) identification numbers and disease

status (type 1 diabetes (T1D), autoantibody positive (Ab+), and no diabetes (control)) are listed in the far left two columns. Each subsequent column represents an assay utilized herein, and an X indicates that the assay was performed. For some donors, tissue availability restricted our ability to perform all assays; hence, empty cells indicate assays that were not performed for a specific donor.

Table S2, Related to Figure 2. For autoantibody positive (Ab+) donors, Network for Pancreatic Organ Donors with Diabetes (nPOD) donor identification numbers, number of Ab detected, and Ab reactivities against insulin (IAA), glutamic acid decarboxylase (GADA), insulinoma associated protein-2 (IA-2A), and Zinc transporter 8 (ZnT8A).

nPOD ID	Detected Ab (N)	Ab reactivities
6027	1	ZnT8A
6044	1	GADA
6080	2	GADA, IAA
6090	1	GADA
6123	1	GADA
6147	1	GADA
6151	1	GADA
6154	1	GADA
6156	1	GADA
6158	2	GADA, IAA
6167	2	IA-2A, ZnT8A
6170	1	GADA
6171	1	GADA
6181	1	GADA
6184	1	GADA
6197	2	GADA, IA-2A

Table S3, Related to STAR Methods. Primers used for qPCR analyses are listed along with the corresponding gene and accession number (Accession #): Carboxypeptidase E (CPE), glucagon (GCG), islet amyloid polypeptide (IAPP), insulin (INS), unspliced heterogeneous nuclear RNA for insulin (INS hnRNA), insulin-insulin like growth factor 2 read through transcript (INS-IGF2), Proprotein Convertase Subtilisin/Kexin Type 1 (PCSK1), Proprotein Convertase Subtilisin/Kexin Type 2 (PCSK2) and somatostatin (SST).

GENE	FORWARD	REVERSE	ACCESSION #
CALM1 hnRNA	GGAACTTGGAACTGTCATGAGG	GGCCCTCATTCATGGTTTTAAAGC	NG_013338.1
CPE	GTGAATGAGAAAGAAGGTGGTCC	TGGCAGAAAGCACAAAAGGA	NM_001873.3
CTRC hnRNA	CCACTCACCCTCTCCACTTTG	GTGACATAGCAGGGGTAGTCC	NG_009253.1
GCG	GAGGAAGGCGAGATTTCCCAG	CCTGGCGGCAAGATTATCAAG	NM_002054.4
IAPP	AAGCAATGGGCATCCTGAAG	CGTTGGTAGATGAGAGAATGGC	NM_000415.2
IFNγ	ATTGGAAAGAGGAGAGTGACAGAA	TGCTTTGCGTTGGACATTCAA	NM_000619.2
IL1β	TCTGGGATTCTCTTCAGCCAATC	CCTCATTGCCACTGTAATAAGCC	NM_000576.2
INS	TCTACACACCCAAGACCCGC	CCACAATGCCACGCTTCTG	NM_000207.2
INS hnRNA	GAGATGGGGAAGATGCTGGG	GGAGGACACAGTCAGGGAGA	NG_007114.1
INS-IGF2	TCTACACACCCAAGACCCGC	ATTAGCAGTCACCACCAAAGCAG	NM_001042376.2

PCSK1	AGCTGGACCTTCATGTGATACC	GCTAGCCTCTGGATCATAGTTGG	NM_000439.4
PCSK2	GCAACGACCCCTATCCTTACC	TGCAACCTTGGAGTTGTATGC	NM_002594.4
PPIA hnRNA	AGAACTTCATCCTAAAGCATACGG	AAAAGTAGTGTTTGTTCCGTTCCC	NG_029697.1
SPINK1 hnRNA	CACCTGGCTCCTTTCACCTT	CCGCACTTACCACGTCTCTT	NG_0083556.2
SST	GATGCTGTCCTGCCGCC	TCTCCGTCTGGTTGGGTTCA	NM_001048.3
TNFα	ACCTCTCTCTAATCAGCCCTCT	CAGCTTGAGGGTTTGCTACAAC	NM_000594.3